The peptide-GPCR project: identification of evolutionary conserved neuropeptide systems in *C. elegans*

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Neuropeptides represent a large and diverse group of signaling molecules that are mainly produced by neurosecretory cells. They may act as fast neurotransmitters, neuromodulators or neurohormones, thereby regulating fundamental physiological processes such as feeding, locomotion, reproduction, social behavior and learning and memory formation. The *C. elegans* genome contains at least 120 neuropeptide precursor genes encoding more than 250 bioactive peptides. The majority of neuropeptides exert their function by binding to plasma membrane-associated receptors known as G-protein coupled receptors (GPCRs), of which about 150 receptor genes have been predicted in *C. elegans*. Coupling of the putative receptors and their natural ligand(s) remains a challenging task, reflected by the small number of peptide GPCRs being deorphanized so far. We have therefore set up the peptide-GPCR project (https://worm.peptide-gpcr.org), a large-scale initiative that aims at pairing all predicted *C. elegans* peptide GPCRs with their cognate neuropeptide ligand(s). Using a reverse pharmacology approach, orphan receptors are heterologously expressed in cells and used as targets to screen a library of more than 300 peptides (based on peptidomics data and *in silico* predictions). In this way, we have identified several evolutionary conserved neuropeptide systems in *C. elegans* including a pathway related to mammalian neuropeptide Y (NPY) and insect neuropeptide F (NPF) signaling. In order to gain clues as to the biological function of this neuropeptide signaling system, the spatial expression of the NPY/F precursor and receptor genes was examined using fluorescent reporter constructs. These expression patterns suggest a role for NPY/F signaling in the regulation of feeding behavior in *C. elegans*.